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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,710	12/22/2000	San Ming Wang	ARCD:343US	4543

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TUNG, JOYCE	
ART UNIT	PAPER NUMBER
1637	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/748,710	Wang et al.
Examiner	**Art Unit**
Joyce Tung	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-41 is/are pending in the application.

4a) Of the above, claim(s) 21-41 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-20 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 1-41 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9-11
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-20, drawn to a method for characterizing a SAGE tag fragment, classified in class 435, subclass 91.51.

   II. Claims 21-31, drawn to a method of identifying a gene, classified in class 435/530, subclass 91.2/305.

   III. Claims 32-41, drawn to a method of characterizing a SAGE tag fragment, classified in class 435, subclass 91.52.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I-III are distinct because they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Group I, claims 1-20 is for characterizing a SAGE tag involving amplifying cDNA from RNA sample with a sense primer and antisense primer, Group II, claims 22-31 are drawn method to identify gene involving protein isolation, digesting the protein, obtaining a first amino acid sequence and generation a first DNA sequence encoding the amino acid sequence and performing DNA amplification with a sense primer and antisense primer and Group III, claims 32-41 is for characterizing a SAGE tag involving a first amplification of cDNA from RNA sample with a 3' anchored oligo dT primer and second amplification of the 3' cDNA fragment from the first cDNA amplification involving ligation a SAGE linker to the 3' cDNA

and amplifying the linked cDNA with a sense primer and antisense primer. Based upon the analysis above, they have different modes of operation, different functions, or different effects. Thus they are distinct inventions.

3. Because these inventions are distinct for the reasons given above and the search required for each group is different, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Mr William Merkel on 3/14/2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-20. Affirmation of this election must be made by applicant in replying to this Office action. Claims 21-41 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Sequence Rules

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth as follows:

All nucleic acid sequences in the specification are required to have SEQ ID NO, for example pg. 7, line 14.

APPLICANT IS GIVEN THE RESPONSE PERIOD SET FORTH IN THIS OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821-1.825. Failure to comply with these requirements will result in **ABANDONMENT** of the application under 37 CFR 1.821(g).

Claim Rejections - 35 USC § 112

7 The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8 Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-20 are failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because it is unclear what is meant by the phrase "cDNA fragments that correspond to the SAGE tag". Does it meant that the cDNA fragments are identical to the SAGE tag or complementary to the SAGE tag.

(b) Claim 5 is vague and indefinite because of the phrase "the Mg^{2+} concentration is 4mM" which has no antecedent basis.

(c) Claim 7 is vague and indefinite because of the phrase "said base excluding dT". Since the claim language addresses that the primer is single-base anchored oligo-dT primer, it is unclear how the dT is excluded.

(d) Claim 13 is vague and indefinite because of the phrase "sequence in existing DNA databases. It is unclear what is the sequence in the existing DNA databases.

(f) Claims 15 and 20 are vague and indefinite because the phrase "the full-length cDNA" has no antecedent basis.

Claim Rejections - 35 USC § 103

9 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-3, 5-9, 11-12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. (Nucleic Acids Research, 1999, Vol. 27 (17), pg. I-iii (e17)) in view of Liang et al. (Nucleic Acids Research, 1994, Vol. 22(25), pg. 5763-5764).

Berg et al. disclose a method of serial analysis of gene expression. The method applies tag specific primer consisted of 10 nucleotides identified in the SAGE analysis with a 5' *Nla* III restriction site and 5' tail of the oligo(dT) primer (See pg. I, column 2, last paragraph). The PCR products obtained are about 50-600 base pairs in length (See pg ii, Table I). The poly-dT residues are 24 dT (See pg. I, column 2, third paragraph). Berg et al. also disclose that the tag-PCR products can be sequenced to obtained gene-specific sequence information, to isolate full-length cDNA clones and to analyse gene expression in various tissues using an RNA in situ hybridization (See pg. iii, column 2, first paragraph). Berg et al. disclose that optimization of the PCR was performed by testing different PCR buffers of which the $MgCl_2$ concentration varied. The test is to predict the tag which was present at predicted location (down stream of the most 3' *Nla* III site in the full length cDNA) (See pg. ii, column 1, first paragraph). This teaching suggests that full-length of cDNA is produced.

Berg et al. do not explicitly disclose that the Mg^{2+} concentration used is 4mM and do not disclose one single-base anchored oligo-dT primer used in the reaction.

Liang et al. disclose a method of identifying and analyzing altered gene expression at the mRNA level in any eukaryotic cell in which one single-base anchored oligo-dT primer is used (See pg. 5763, column 1, second and third paragraph).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Berg et al. by using one single base anchored oligo-dT primer as taught by Liang et al.. The motivation is that one base anchored oligo-dT primer provides excellent selectivity in subdividing mRNA, minimizes the redundancy and under-representation of certain RNA species due to the degeneracy of the primers and more efficient in cDNA amplification while allowing the cloned cDNA to be more readily manipulated (See pg. 5763, column 1, second paragraph). Therefore, it would have been prima facie obvious to characterize a SAGE tag fragment recited in claim 1 with using one single-base anchored oligo-dT primer.

Moreover, one of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Berg et al. by using the Mg^{2+} concentration which is 4mM. The motivation is that the optimization of the PCR was performed by testing different PCR buffers of which the $MgCl_2$ concentration varied to predict the tag which was present at predicted location (down stream of the most 3' *Nla* III site in the full length cDNA) (See pg. ii, column 1, first paragraph). Thus, it would have been prima facie obvious to use the Mg^{2+} concentration which is 4mM in a method of characterizing a SAGE tag fragment.

11. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. (Nucleic Acids Research, 1999, Vol. 27 (17), pg. I-iii (e17)) in view of Liang et al. (Nucleic Acids Research, 1994, Vol. 22(25), pg. 5763-5764) as applied to claims 1-3, 5-9, 11-12, and 15 above, and further in view of Lundberg et al. (Gene, 1991, Vol. 108, pg. 1-6).

The teachings of Berg et al. and Liang et al. are set forth in section 10 above.

None of these references above discloses using *Pfu* DNA polymerase

Lundberg et al. disclose using *Pfu* DNA polymerase for polymerase chain reaction. *Pfu* DNA polymerase yields amplification products containing less than 10% of the number of mutations obtained from amplification performed with *Taq* DNA polymerase (See pg. 1, the abstract).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Van Den Berg et al. by using *Pfu* DNA polymerase. The motivation is the benefit of using *Pfu* DNA polymerase in amplification as discussed above. It would have been prima facie obvious to apply *Pfu* DNA polymerase in the method recited in claim 1.

12. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. (Nucleic Acids Research, 1999, Vol. 27 (17), pg. I-iii (e17)) in view of Liang et al. (Nucleic Acids Research, 1994, Vol. 22(25), pg. 5763-5764) as applied to claims 1-3, 5-9, 11-12, and 15 above, and further in view of Spinella (6,461,814).

The teachings of Berg et al. and Liang et al. are set forth in section 10 above.

None of these references above discloses that the sense primer comprises a *Bam* HI. recognition sequence at the 5' end.

Spinella discloses a method of obtaining short DNA tag involving a 5' adapter contained a restriction sequence for a 5' cloning restriction endonuclease (BamH1)(See column 3, lines 53-59).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Berg et al. by using a sense primer comprising a *Bam* H1

recognition sequence at the 5' end because the recognition sequence of *Bam* H1 at its 5' end facilitate later cloning (See column 9, lines 1-10). It would have been prima facie obvious to use a sense primer with the recognition sequence of *Bam* H1 at its 5' end in the method of characterize SAGE tag fragment, further the method of characterizing SAGE tag fragment of instant invention includes cDNA cloning steps.

13. Claims 13-14, 18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. (Nucleic Acids Research, 1999, Vol. 27 (17), pg. I-iii (e17)) in view of Liang et al. (Nucleic Acids Research, 1994, Vol. 22(25), pg. 5763-5764) as applied to claims 1-3, 5-9, 11-12 and 15 and further in view of Velculescu et al. (Science, 1995, Vol. 270(20), pg. 484-487).

The teachings of Berg et al. and Liang et al. are set forth in section 10 above.

None of these references above discloses comparing the cDNA sequence to sequence existing DNA database, hybridizing to the cDNA with known sequence to identify the cDNA fragment, cDNA cloned into an expression vector and aligning the sequence of the amplified cDNA with genomic DNA sequence.

Velculescu et al. disclose a method of SAGE to analyze a large number of transcripts (See pg. 484, the abstract). The ditag is amplified by polymerase chain reaction (See pg. 485, column 1) and then were cloned into a plasmid vector. The clones containing tags were identified by manually sequenced (See pg. 485, column 3). The quantitative nature of SAGE was evaluated by cDNA library that was screened with cDNA probes. Comparison of transcript abundance was also presented as determined by SAGE or hybridization analysis (See pg. 485, column 3, fig. 2).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Berg et al. by applying the cloning ditag, sequencing ditag and hybridization analysis of ditag as taught by Velculescu et al. because by using these techniques, SAGE provides a broadly applicable means for quantitative cataloging and comparison of expressed genes in a variety of normal, developmental and disease states (See 484, the abstract). It would have been prima facie obvious to apply the cloning ditag, sequencing ditag and hybridization of analyzing ditag to the method of characterizing SAGE tag fragment.

14. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al. (Nucleic Acids Research, 1999, Vol. 27 (17), pg. I-iii (e17)) in view of Liang et al. (Nucleic Acids Research, 1994, Vol. 22(25), pg. 5763-5764) as applied to claims 1-3, 5-9, 11-12, and 15 above, and further in view of Velculescu et al. (Nature Genetics, 1999, Vol. 23, pg. 387-388).

The teachings of Berg et al. and Liang et al. are set forth in section 10 above.

None of these references above discloses the tissue used in the method of characterizing SAGE fragment recited in claim 1, for example, colon, prostate and lung.

Velculescu et al. disclose serial analysis of gene expression studies of 84 libraries derived from 19 different sources identified 134,135 transcripts from approximately 84,000 different genes (See pg. 387, table 1).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Berg et al. by applying the method to the tissues of colon, prostate and lung because Velculescu et al. applied serial analysis of gene expression to many types tissues as listed in table 1 (See pg. 387, table 1). Regardless of type of tissue used, serial

analysis of gene expression (SAGE) provides absolute rather than relative expression levels and SAGE data can be directly integrated with those described here to provide progressively deeper insights into expression patterns. It would have been prima facie obvious to apply the instant method of characterizing SAGE fragment to colon, prostate and lung tissues.

Summary

15. No claims are allowable.

16. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

March 20, 2003

Jeffrey Siew

JEFFREY SIEW
PRIMARY EXAMINER

3/24/03